

## **CHEMICAL MEETING THE CRITERIA FOR LISTING AS CAUSING CANCER VIA THE AUTHORITATIVE BODIES MECHANISM**

### **PACKAGE 19a.1.a**

**February 9, 2001**

Reproductive and Cancer Hazard Assessment Section  
Office of Environmental Health Hazard Assessment  
California Environmental Protection Agency

The chemical listed in the table below meets the criteria for listing under Proposition 65 via the authoritative bodies listing mechanism. The regulatory guidance for listing by this mechanism is set forth in Title 22, California Code of Regulations (CCR), Section 12306. For example, the regulations include provisions covering the criteria for evaluating the documentation and scientific findings by the authoritative body to determine whether listing under Proposition 65 is required.

The U.S. Environmental Protection Agency (U.S. EPA) is one of five institutions which has been identified as an authoritative body for the purposes of Proposition 65 (22 CCR 12306(l)). U.S. EPA has identified the chemical in the table below as causing cancer. The Office of Environmental Health Hazard Assessment (OEHHA) has found that this chemical appears to be “formally identified” as causing cancer according to the regulations covering this issue (22 CCR 12306(d)). The chemical below is the subject of a report published by the authoritative body which concludes that the chemical causes cancer. Also, the document specifically and accurately identifies the chemical and meets one or more of the criteria outlined in 22 CCR 12306(d)(2).

OEHHA also finds that the criteria given in regulation for “as causing cancer” (22 CCR 12306(e)) have been satisfied for the chemical in the table below. In making this evaluation, OEHHA relied upon the discussion of data by the authoritative body in making its findings that the specified chemical causes cancer. A brief discussion of the relevant carcinogenesis studies providing evidence for the finding is presented below. The statement in bold reflects data and conclusions that satisfy the criteria for the sufficiency of evidence for carcinogenicity (22 CCR 12306(e)). The full citation for the authoritative body document is given in this report.

**Chemical Meeting the Criteria for Listing as Causing Cancer**

<b>Chemical</b>	<b>CAS No.</b>	<b>Chemical Use</b>	<b>Reference</b>
Bromate	-----	Chemical by-product, produced by ozonation of water containing bromide.	U.S. EPA (1998a, b)

Bromate

**Increased incidence of malignant and combined malignant and benign tumors in male and female rats; in males, tumors were observed at multiple sites in multiple experiments.**

In a final rule for bromate, U.S. EPA (1998a) stated that “there is sufficient laboratory animal data to conclude that bromate is a probable (likely under the 1996 proposed cancer guidelines) human carcinogen.” The U.S. EPA had classified bromate as a Group B2 carcinogen in 1993 (U.S. EPA, 1993). This finding was also stated in a 1998 Health Risk Assessment (U.S. EPA, 1998b) which concluded “bromate should be evaluated as a likely human carcinogen by the oral route of exposure.” The studies upon which U.S. EPA based its findings are described below.

In the first study (Kurokawa *et al.*, 1986a), male F344 rats were treated with water containing potassium bromate for 104 weeks. There were statistically significant increases in tumors at multiple sites. The combined incidences of adenoma and carcinoma of the kidney were significantly increased in animals in the two highest of six dose groups ( $p < 0.001$  and  $p < 0.05$  for the highest and next highest dose groups, respectively). Thyroid follicular cell adenomas and carcinomas combined were significantly increased in the high-dose group ( $p < 0.05$ ) as were peritoneal mesotheliomas ( $p < 0.05$ ). In the second set of studies (Kurokawa *et al.*, 1986b), bromate was administered in drinking water to male and female F344 rats and female B6C3F<sub>1</sub> mice. In male rats, there were statistically significant increases in renal carcinoma (3/53, 24/53, and 44/52 for control, low- and high-dose groups, respectively), combined renal adenomas and carcinomas (3/53, 32/53, 46/52), and peritoneal mesotheliomas (6/53, 17/52, 28/46). In female rats, statistically significant increases in renal carcinoma (0/47, 21/50, 36/49) and renal adenomas and carcinoma combined (0/47, 28/50, 39/49) were observed. Results in mice were inconclusive.

In the third set of studies (DeAngelo *et al.*, 1998), potassium bromate was administered to male F344 rats and male B6C3F<sub>1</sub> mice in drinking water for 100 weeks. In treated male rats, statistically significant increases in renal tumors (carcinomas: 0/45, 0/43, 2/47, 1/39, 4/32; combined adenomas/carcinomas: 1/45, 1/43, 6/47, 3/39, 12/32); thyroid tumors (carcinomas: 0/36, 2/39, 0/43, 2/35, 6/30; combined adenomas/carcinomas: 0/36, 4/39, 1/43, 4/35, 14/30); and testicular mesotheliomas (0/47, 4/49, 5/49, 10/47, 27/43) were

observed. Mice appeared to be less sensitive than rats to the effects of bromate exposure. In male mice, kidney tumors were observed but the incidence was not dose-dependent. U.S. EPA (1998a) also noted that bromate has been found to be mutagenic in both *in vitro* and *in vivo* assays.

In all of the cited studies, bromate was administered as potassium bromate. Potassium bromate was listed as causing cancer under Proposition 65 on January 1, 1990. Potassium bromate is readily soluble in water. At drinking water pH, it should exist almost exclusively in the ionic form. Thus, U.S. EPA refers to dose of bromate in its documents and characterizes the potential for carcinogenicity following bromate exposure (U.S. EPA, 1993; 1998a; b).

## **REFERENCES**

DeAngelo AB, George MH, Kilburn SR, Moore TM, Wolf DC (1998). Carcinogenicity of Potassium Bromate Administered in the Drinking Water of Male B6C3F<sub>1</sub> Mice and F344/N Rats. *Toxicol Path* **26**:587-594.

Kurokawa Y, Aoki S, Matsushima Y, Takamura N, Imazawa T, Hayashi Y (1986a). Dose-Response Studies on the Carcinogenicity of Potassium Bromate in F344 Rats After Long-Term Oral Administration. *J Natl Cancer Inst* **77**:977-982.

Kurokawa Y, Takayama S, Konishi Y, Hiasa Y, Asahina S, Takahashi M, Maekawa A, Hayashi Y (1986b). Long-Term In Vivo Carcinogenicity Tests of Potassium Bromate, Sodium Hypochlorite and Sodium Chlorite Conducted in Japan. *Environ Health Persp* **69**:221-236.

U.S. Environmental Protection Agency (U.S. EPA, 1993). *Final Draft for the Drinking Water Criteria Document on Bromate*. Prepared for the Health and Ecological Criteria Division, Office of Science and Technology, Office of Water by Clement International Corporation. September 30, 1993.

U.S. Environmental Protection Agency (U.S. EPA, 1998a). National Primary Drinking Water Regulations: Disinfectants and Disinfection Byproducts; Final Rule. December 16. *Federal Register* **63**(241):69389-69476.

U.S. Environmental Protection Agency (U.S. EPA, 1998b). *Health Risk Assessment/Characterization of Drinking Water Disinfection Byproduct Bromate*. Health and Ecological Criteria Division, Office of Science and Technology, Office of Water, U.S. EPA, Washington, D.C.